Amendments to the Specification:

Please replace the paragraph beginning at page 1, paragraph [001] with the following rewritten paragraph:

~~--This application claims benefit of priority under 35 USC 119(e)(1) to USSN: 60/415,541, filed October 1, 2002; USSN: 60/477,246, filed June 10, 2003, and 60/489,725, filed July 24, 2003, and 10/676,705, filed September 30, 2003, all hereby incorporated by reference in their entirety.~~ This application is a continuation-in-part application of U.S.S.N. 10/676,705 filed September 30, 2003 which claims the benefit of the filing date under 35 U.S.C. § 119(e) of U.S.S.N. 60/415,541 filed October 1, 2002, U.S.S.N. 60/477,246 filed June 10, 2003, and U.S.S.N. 60/489,725 filed July 24, 2003.--

Please replace the paragraph beginning at page 5, paragraph [032] with the following rewritten paragraph:

--Preferred variants in agretope 6 include SEQ ID NOS:~~**1-14~~150-163. Preferred variants in agretope 8 include SEQ ID NOS:~~**15-45~~164-194. Preferred variants in agretope 11 include SEQ ID NOS:~~**46-54~~ 195-203. Preferred variants in agretope 20 include SEQ ID NOS:~~**55-65~~204-214. Preferred variants in agretope 24 include SEQ ID NOS:~~**66-100~~215-249. A preferred variants in agretope 25 includes SEQ ID NO: ~~**101~~250.--

Please replace the paragraph beginning at page 6, paragraph [040] with the following rewritten paragraph:

--Figures1A-D shows amino acid sequences for human type I interferons and some preferred variants SEQ ID NOS:1-30.--

Please replace the paragraph beginning at page 6, paragraph [041] with the following rewritten paragraph:

-- Figure 2 shows a sequence alignment of human interferon-alpha subtypes, SEQ ID NOs:31-~~43~~44.--

Please replace the paragraph beginning at page 6, paragraph [042] with the following rewritten paragraph:

--Figure 3 shows the sequence alignment of IFN-a2a (1ITF), IFN-b (1AU1), IFN-k (IFNK), and IFN-t (1B5L) (SEQ ID NOs:44-~~47~~48) that was used to construct the homology model of interferon-kappa.--

Please replace the paragraph beginning at page 7, paragraph [050] with the following rewritten paragraph:

--Figures 11A-C graphically shows decreased aggregation of SEQ ID NO: 20 variant as compared to BetaSeron® (Schering AG/Berlex) at pH 3.0 over time (9h at 37°C). ~~The top graph~~ Figure 11A shows XENP806, ~~the middle graph~~Figure 11B shows BetaSeron and ~~the bottom graph~~Figure 11C shows wild type IFNB.--

Please replace the paragraph beginning at page 7, paragraph [051] with the following rewritten paragraph:

--Figure 12 graphically shows decreased aggregation of SEQ ID NO: 20 variant as compared to BetaSeron® (Schering AG/Berlex) at 6 pH 6.0 ± 1.0 over time (9h at 37°C). ~~The top graph~~Figure 12A shows XENP806, ~~the middle graph~~Figure 12B shows BetaSeron and ~~the bottom graph~~ Figure 12C shows wild type IFNB.--

Please replace the paragraph beginning at page 17, paragraph [096] with the following rewritten paragraph:

--In one embodiment, the library is a combinatorial library, meaning that the library comprises all possible combinations of allowed residues at each of the variable positions. For example, if positions 3 and 9 are allowed to vary, allowed choices at position 3 are A, V, and I, and allowed choices at position 9 are E and Q, the library includes the following sequences: 3A/9E, 3A/9Q, 3V/9E, 3V/9Q, 3I/9E, and 3I/9Q. In a preferred embodiment, PDA® technology calculations may be used to modify wild type interferon sequences to generate novel, non-naturally occurring, soluble proteins from known interferon sequences (see for example, ~~Figure 1~~ Figures 1A-D). See US 6,188,965; US 6,269,312; US 6,403,312, expressly incorporated by reference herein.--

Please replace the paragraph beginning at page 30, paragraph [0185] with the following rewritten paragraph:

--*Combining immunogenicity reduction strategies* In a preferred embodiment, more than one method is used to generate variant proteins with desired functional and immunological properties. For example, substitution matrices may be used in combination with PDA® technology calculations. Strategies for immunogenicity reduction include, but are not limited to, those described in US.S.N.

10/822,231, Optimized Fc Variants and Methods for Generation, filed March 26, 2004, incorporated by reference.--

Please replace the paragraph beginning at page 30, paragraph [0187] with the following rewritten paragraph:

--In an additional preferred embodiment, a variant protein with reduced binding affinity for one or more class II MHC alleles is further modified by derivitization with PEG or another molecule. As is known in the art, PEG may sterically interfere with antibody binding or improve protein solubility, thereby reducing immunogenicity. In an especially preferred embodiment, rational PEGylation methods are used (see U.S.S.N. 60/459,094 and U.S.S.N. 10/811,492, "Generating Protein ProDrugs using Reversible PPG Linkages, filed 3/19/04, hereby incorporated by reference).--

Please replace the paragraph beginning at page 30, paragraph [0190] with the following rewritten paragraph:

--In a preferred embodiment, the immunogenicity of interferons may be modulated. See for example USSNs: 09/903,378; 10/039,170; 10/339,788 (filed January 8, 2003, titled Novel Protein with Altered Immunogenicity); and PCT/US01/21823; and PCT/US02/00165. All references expressly incorporated by reference in their entirety. See for example USSNs: 09/903,378; 10/039,170; 10/339,788 (filed January 8, 2003, titled Novel Protein with Altered Immunogenicity); and PCT/US01/21823; and PCT/US02/00165. All references cited herein are expressly incorporated by reference in their entirety.--

Please replace the paragraph beginning at page 43, paragraph [0258] with the following rewritten paragraph:

--A homology model of interferon kappa was constructed based on the sequence of human interferon kappa (GenBank code 14488028(SEQ ID NO:16)), the crystal structures for interferon tau (PDB code 1BL5) and interferon beta (PDB code 1AU1), as well as the NMR structure for interferon alpha-2a (PDB code 1ITF). The sequences for interferons alpha-2a, beta, kappa, and tau were aligned using the multiple sequence alignment tool in the Homology model of the InsightII software package (Accelrys), as shown in Figure 2. As the sequences share only approximately 35% identity, slightly different sequence alignments could have been used instead (see for example LaFleur et. al. J. Biol. Chem. 276: 39765-39771 (2001)). Based on similarity to the other interferon sequences, disulfide bonds are expected to be formed between residues C3 and C102 and between residues C32 and C155 (LaFleur supra); these

disufides were used as constraints in the generation of the homology models. A total of nine homology models were generated using the Modeler tool in the InsightII software package (Accelrys). The structures were analyzed for quality and the top four models were used in the analysis and design calculations described below.--

Please replace the paragraph beginning at page 78, paragraph [0313] with the following rewritten paragraph:

--*Construction of the interferon beta gene as a template for mutagenesis.* The DNA sequence, GenBank accession number NM_002176(SEQ ID NO:273), encompassing the full-length human interferon beta cDNA gene containing the native signal sequence was modified to remove the signal sequence and facilitate high level expression in bacterial cells. Primers were designed to synthesize the region between positions 65-561 by recursive PCR. The primer sequences also biased the codon usage towards highly expressed *E. coli* bacterial genes. In addition, the codon for cysteine 17 (amino acid numbering with the signal sequence removed) was changed to serine. An internal SacI DNA restriction enzyme site was designed for ease of later mutagenesis as well as NdeI and XhoI restriction sites flanking the ends of the gene for cassette cloning into various expression vectors. The bacterial expression vectors pET28a and pET24a (Novagen) were used to sub-clone the interferon beta gene containing C17S between the NdeI and XhoI multiple cloning restriction sites. Cloning into pET24a expression in *E. coli* produces a C17S interferon beta variant while cloning into pET28a introduces the additional amino acid sequence MGSSHHHHHHSSGLVPRGSH (SEQ ID NO:274) to the N-terminus of C17S. This amino acid sequence includes a 6-His purification tag and a thrombin cleavage site for later removal of the added amino acid sequences.--

Please replace the paragraph and table 20 beginning at page 81, paragraph [0326] with the following rewritten paragraph and table 20:

--**Table 20:** Amino acid sequences at exposed hydrophobic positions for active interferon beta variants

		Amino acid position					
SEQ ID NO	Variant	5	8	47	111	116	120
SEQ ID NO:49	IFB1_2	Q	F	L	F	L	L
SEQ ID NO:50	IFB1_3	Q	F	K	F	L	L

SEQ ID NO:51	IFB1_4	L	E	L	F	L	L
SEQ ID NO:52	IFB1_5	L	E	K	F	L	L
SEQ ID NO:53	IFB1_6	L	F	K	F	L	L
SEQ ID NO:54	IFB1_7	Q	E	L	F	L	L
SEQ ID NO:55	IFB1_8	Q	E	K	F	L	L
SEQ ID NO:56	IFB1_9	L	F	L	N	L	L
SEQ ID NO:57	IFB1_10	Q	F	L	N	L	L
SEQ ID NO:58	IFB1_11	Q	F	K	N	L	L
SEQ ID NO:59	IFB1_15	Q	E	L	N	L	L
SEQ ID NO:60	IFB1_16	Q	E	K	N	L	L
SEQ ID NO:61	IFB1_23	Q	E	L	F	E	L
SEQ ID NO:62	IFB1_26	Q	F	L	F	L	R
SEQ ID NO:63	IFB1_27	Q	F	K	F	L	R
SEQ ID NO:64	IFB1_28	L	E	L	F	L	R
SEQ ID NO:65	IFB1_29	L	E	K	F	L	R
SEQ ID NO:66	IFB1_31	Q	E	L	F	L	R
SEQ ID NO:67	IFB1_32	Q	E	K	F	L	R
SEQ ID NO:68	IFB1_33	L	F	L	N	E	L
SEQ ID NO:69	IFB1_34	Q	F	L	N	E	L
SEQ ID NO:70	IFB1_35	Q	F	K	N	E	L
SEQ ID NO:71	IFB1_36	L	E	L	N	E	L
SEQ ID NO:72	IFB1_37	L	E	K	N	E	L
SEQ ID NO:73	IFB1_39	Q	E	L	N	E	L
SEQ ID NO:74	IFB1_40	Q	E	K	N	E	L
SEQ ID NO:75	IFB1_41	L	F	L	N	L	R
SEQ ID NO:76	IFB1_42	Q	F	L	N	L	R
SEQ ID NO:77	IFB1_44	L	E	L	N	L	R
SEQ ID NO:78	IFB1_47	Q	E	L	N	L	R
SEQ ID NO:79	IFB1_48	Q	E	K	N	L	R
SEQ ID NO:80	IFB1_50	Q	F	L	F	E	R
SEQ ID NO:81	IFB1_51	Q	F	K	F	E	R
SEQ ID NO:82	IFB1_52	L	E	L	F	E	R

SEQ ID NO:83	IFB1_55	Q	E	L	F	E	R
SEQ ID NO:84	IFB1_56	Q	E	K	F	E	R
SEQ ID NO:85	IFB1_63	Q	E	L	N	E	R
SEQ ID NO:86	IFB1_64	Q	E	K	N	E	R

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Please replace the paragraph beginning at page 82, paragraph [0329] with the following rewritten paragraph:

--The sequence for residues 5, 8, 47, 111, 116, and 120 is given for each variant, along with the total number of mutations, the EC50, and the ratio of the wild type to variant EC50. Variant IFN1_1 is the interferon beta wild type with C17S.

SEQ ID NO	Variant	5	8	47	111	116	120	# mut	EC50 (log ng/ml)	EC50 wt / EC50 var
SEQ ID NO:15	IFN1_1	L	F	L	F	L	L	0	5.306	1.0
SEQ ID NO:49	IFB1_2	Q	F	L	F	L	L	1	0.428	12.4
SEQ ID NO:54	IFB1_7	Q	E	L	F	L	L	2	0.179	29.6
SEQ ID NO:59	IFB1_15	Q	E	L	N	L	L	3	0.319	16.6
SEQ ID NO:61	IFB1_23	Q	E	L	F	E	L	3	0.277	19.2
SEQ ID NO:71	IFB1_36	L	E	L	N	E	L	3	0.294	18.0
SEQ ID NO:73	IFB1_39	Q	E	L	N	E	L	4	0.193	27.5
SEQ ID NO:86	IFB1_64	Q	E	K	N	E	R	6	0.240	22.1

--

Please replace the paragraph and table beginning at page 83, paragraph [0333] with the following rewritten paragraph and table:

--The sequence for residues 5, 8, 47, 50, 106, 111, 116, and 120 is given for each variant, along with the total number of mutations, the EC50, and the ratio of the wild type to variant EC50. All variants are in the C17S background.

SEQ ID NO	Variant	5	8	47	50	106	111	116	120	# mut	EC50 (ng/ml)	EC50 wt / EC50 var
SEQ ID NO:15	IFN1_1	L	F	L	F	L	F	L	L	0	1.90	1.00

SEQ ID NO:54	IFB1_7	Q	E	L	F	L	F	L	L	2	0.074	25.7
SEQ ID NO:87	IFB_GM2	L	F	S	S	S	S	S	S	6	130	0.015

--

Please replace the paragraph and table beginning at page 84, paragraph [0342] with the following rewritten paragraph and table:

--**Table 24.** Sequence analysis of selected interferon kappa variants with improved soluble expression.

SEQ ID NO:88	WT Seq	L-V	W	F-V	I	Y-M	F-Y	I	Y	V	C-Y-Y
	Mutation	Q-N	R	Q-R	N	Q-N	S-A	T	D	A	A-S-T
	Mutant	5, 8	15	28, 30	37	48, 52	76, 78	89	97	161	166, 168, 171
SEQ ID NO:89	IK_4-G7	L-N	R	F-V	I	Q-N	S-A	T	Y	V	C-Y-Y
SEQ ID NO:90	IK_12-E4	L-N	R	F-V	I	Q-N	S-A	T	Y	V	C-Y-Y
SEQ ID NO:91	IK_2-C11	L-N	R	Q-R	N	Y-M	S-A	T	D	A	A-S-T
SEQ ID NO:92	IK_10-D8	L-N	W	F-V	I	Q-N	F-Y	T	D	V	A-S-T
SEQ ID NO:93	IK_10-H7	L-N	W	F-V	I	Q-N	S-A	T	D	A	A-S-T
SEQ ID NO:94	IK_20-B12	L-N	W	Q-R	I	Q-N	S-A	T	Y	V	A-S-T
SEQ ID NO:95	IK_3-A11	L-N	W	Q-R	I	Y-M	S-A	T	D	A	A-S-T
SEQ ID NO:96	IK_3-H7	L-N	W	Q-R	I	Y-M	S-A	T	D	A	A-S-T
SEQ ID NO:97	IK_12-F11	L-N	W	Q-R	N	Q-N	S-A	T	Y	V	A-S-T
SEQ ID NO:98	IK_3-D10	L-V	R	F-V	I	Q-N	S-A	T	D	V	A-S-T
SEQ ID NO:99	IK_3-C10	L-V	R	F-V	I	Q-N	S-A	T	D	V	C-Y-Y
SEQ ID NO:100	IK_3-H11	L-V	R	F-V	I	Q-N	S-A	T	D	V	C-Y-Y
SEQ ID NO:101	IK_21-E1	L-V	R	F-V	I	Y-M	S-A	I	D	V	A-S-T
SEQ ID NO:102	IK_4-H11	L-V	R	F-V	I	Y-M	S-A	T	D	A	C-Y-Y
SEQ ID NO:103	IK_3-A2	L-V	R	F-V	I	Y-M	S-A	T	D	V	A-S-T
SEQ ID NO:104	IK_10-D2	L-V	R	F-V	N	Y-M	S-A	T	D	V	C-Y-Y
SEQ ID NO:105	IK_12-H4	L-V	W	F-V	I	Q-N	S-A	I	Y	V	C-Y-Y
SEQ ID NO:106	IK_27-A6	L-V	W	F-V	I	Q-N	S-A	T	D	A	C-Y-Y
SEQ ID NO:107	IK_2-B4	L-V	W	F-V	I	Q-N	S-A	T	D	V	C-Y-Y
SEQ ID NO:108	IK_3-F11	L-V	W	F-V	I	Q-N	S-A	T	D	V	C-Y-Y
SEQ ID NO:109	IK_14-A9	L-V	W	F-V	I	Y-M	F-Y	T	Y	V	C-Y-Y

SEQ ID NO:110	IK_19-A5	L-V	W	F-V	I	Y-M	S-A	I	D	A	C-Y-Y
SEQ ID NO:111	IK_3-G10	L-V	W	F-V	I	Y-M	S-A	I	D	V	C-Y-Y
SEQ ID NO:112	IK_4-A2	L-V	W	F-V	I	Y-M	S-A	I	D	V	C-Y-Y
SEQ ID NO:113	IK_4-A10	L-V	W	F-V	I	Y-M	S-A	I	D	V	C-Y-Y
SEQ ID NO:114	IK_16-G2	L-V	W	F-V	I	Y-M	S-A	T	D	A	C-Y-Y
SEQ ID NO:115	IK_22-A4	L-V	W	F-V	I	Y-M	S-A	T	D	V	A-S-T
SEQ ID NO:116	IK_1-C8	L-V	W	F-V	N	Q-N	S-A	I	D	V	C-Y-Y
SEQ ID NO:117	IK_23-C10	L-V	W	F-V	N	Q-N	S-A	I	D	V	C-Y-Y
SEQ ID NO:118	IK_12-H11	L-V	W	F-V	N	Q-N	S-A	T	Y	V	C-Y-Y
SEQ ID NO:119	IK_9-H4	L-V	W	Q-R	N	Y-M	S-A	I	D	V	A-S-T

--

Please replace the paragraph and table beginning at page 85, paragraph [0344] with the following rewritten paragraph and table:

--**Table 25.** Sequence analysis of some of the Interferon-kappa variant, which still retain activity, as tested in an ISRE assay as described above for interferon beta.

SEQ ID NO:88	WT seq	L-V	W	F-V	I	Y-M	F-Y	I	Y	V	C-Y-Y
	Mutations	Q-N	R	Q-R	N	Q-N	S-A	T	D	A	A-S-T
	Variant	5, 8	15	28, 30	37	48, 52	76, 78	89	97	161	166, 168, 171
SEQ ID NO:89	IK1_4_G7	L-N	R	F-V	I	Q-N	S-A	T	Y	V	C-Y-Y
SEQ ID NO:120	IK1_46_E2	L-V	R	F-V	N	Q-N	S-A	T	D	A	A-S-T
SEQ ID NO:121	IK1_47_C4	L-V	R	F-V	I	Y-M	S-A	I	Y	V	C-Y-Y
SEQ ID NO:117	IK1_23_C10	L-V	W	F-V	N	Q-N	S-A	I	D	V	C-Y-Y
SEQ ID NO:122	IK1_40_A10	L-V	R	F-V	N	Y-M	S-A	I	Y	V	C-Y-Y

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Please replace the paragraph beginning at page 86, paragraph [0346] with the following rewritten paragraph:

--This experiment evaluated the efficacy of the IFN of the present invention with respect to stability at certain pHs. More specifically, with the purpose of decreasing dimerization and higher order oligomerization of the molecule at pH ranges close to physiological ranges in order to determine aggregation levels. Thus, the relative rates of aggregation of XENP342 (C17S background, SEQ ID NO: ~~31~~ 180) and XENP806 (L5Q/F8E/C17S variant, SEQ ID NO: 20) were measured.--

Please delete the paragraph beginning at page 86, paragraph [0351]:

~~***examples from provisional~~

Please replace the paragraph beginning at page 86, paragraph [0353] with the following rewritten paragraph:

--Matrix method calculations (Sturniolo, supra) were conducted using the parent interferon ~~beta~~ alpha sequence shown in SEQ_ID_NO:1.--

Please replace the paragraph and table beginning at page 86, paragraph [0353] with the following rewritten paragraph and table:

Matrix method calculations (Sturniolo, supra) were conducted using the parent interferon beta sequence shown in ~~SEQ_ID_NO:1~~SEQ ID NO:1.

Please replace the paragraph and table beginning at page 87, paragraph [0356] with the following rewritten paragraph and table:

--**Table 26.** Predicted MHC-binding agretopes in interferon beta. The number of alleles and percent of population hit at 1%, 3%, and 5% thresholds are shown. Especially preferred agretopes are predicted to affect at least 10% of the population, using a 1% threshold.

Table 26. Predicted MHC-binding agretopes in interferon beta.

SEQ ID NO	Agretope number	Residues	Sequence	1% hits	3% hits	5% hits	1% pop	3% pop	5% pop
SEQ ID NO:123	1	3 - 11	YNLLGFLQR	0	0	1	0.0%	0.0%	11.4%
SEQ ID NO:124	2	5 - 13	LLGFLQRSS	0	3	4	0.0%	19.9%	21.2%
SEQ ID NO:125	3	8 - 16	FLQRSSNFQ	0	2	2	0.0%	6.7%	6.7%
SEQ ID NO:126	4	9 - 17	LQRSSNFQC	0	0	2	0.0%	0.0%	7.5%
SEQ ID NO:127	5	15 - 23	FQCQKLLWQ	0	1	1	0.0%	11.4%	11.4%
SEQ ID NO:128	6	22 - 30	WQLNGRLEY	2	3	5	19.3%	20.9%	28.3%
SEQ ID NO:129	7	30 - 38	YCLKDRMNF	0	2	2	0.0%	13.5%	13.5%
SEQ ID NO:130	8	36 - 44	MNFDIPEEI	1	1	1	21.3%	21.3%	21.3%
SEQ ID NO:131	9	47 - 55	LQQFQKEDA	0	0	1	0.0%	0.0%	1.7%
SEQ ID NO:132	10	57 - 65	LTIYEMLQN	0	2	2	0.0%	24.1%	24.1%
SEQ ID NO:133	11	60 - 68	YEMLQNIFA	2	7	7	15.0%	40.2%	40.2%
SEQ ID NO:134	12	63 - 71	LQNIFAIFR	0	1	1	0.0%	5.0%	5.0%
SEQ ID NO:135	13	70 - 78	FRQDSSSTG	0	1	3	0.0%	14.0%	33.5%
SEQ ID NO:136	14	79 - 87	WNETIVENL	0	0	1	0.0%	0.0%	24.7%
SEQ ID NO:137	15	95 - 103	INHLKTVLE	1	1	1	1.8%	1.8%	1.8%

SEQ ID NO:138	16	122 - 130	LKRYYGRIL	0	2	2	0.0%	24.1%	24.1%
SEQ ID NO:139	17	125 - 133	YYGRILHYL	0	0	1	0.0%	0.0%	5.1%
SEQ ID NO:140	18	129 - 137	ILHYLKAKE	1	1	1	5.1%	5.1%	5.1%
SEQ ID NO:141	19	130 - 138	LHYLKAKEY	0	0	1	0.0%	0.0%	5.0%
SEQ ID NO:142	20	143 - 151	WTIVRVEIL	1	1	1	24.7%	24.7%	24.7%
SEQ ID NO:143	21	145 - 153	IVRVEILRN	1	3	5	4.5%	19.7%	39.0%
SEQ ID NO:144	22	146 - 154	VRVEILRNF	0	1	2	0.0%	10.5%	18.5%
SEQ ID NO:145	23	148 - 156	VEILRNFYF	0	1	4	0.0%	5.9%	29.3%
SEQ ID NO:146	24	151 - 159	LRNFYFINR	1	2	2	22.6%	24.1%	24.1%
SEQ ID NO:147	25	154 - 162	FYFINRLTG	1	3	5	11.4%	17.1%	28.3%
SEQ ID NO:148	26	156 - 164	FINRLTGYL	1	1	1	5.1%	5.1%	5.1%
SEQ ID NO:149	27	157 - 165	INRLTGYLR	0	0	1	0.0%	0.0%	5.0%

--

Please replace the paragraph beginning at page 88, paragraph [0371] with the following rewritten paragraph:

--**Table 28.** Suitable less immunogenic variants of agretope 6 (residues 22-30). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 28. Suitable less immunogenic variants of agretope 6 (residues 22-30).

Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:1~~SEQ ID NO:150	WSLNGRLEY	0	48	WQLNGRLEY	53
~~SEQ ID:2~~SEQ ID NO:151	WNLNGRLEY	0	48	WQLNGRLEY	53
~~SEQ ID:3~~SEQ ID NO:152	WDLNGRLEY	0	48	WQLNGRLEY	53
~~SEQ ID:4~~SEQ ID NO:153	WELNGRLEY	0	50	WQLNGRLEY	53
~~SEQ ID:5~~SEQ ID NO:154	WHLNGRLEY	0	48	WQLNGRLEY	53
~~SEQ ID:6~~SEQ ID NO:155	WKVNGRLEY	0	46	WQLNGRLEY	53
~~SEQ ID:7~~SEQ ID NO:156	WQVNGRLEY	0	50	WQLNGRLEY	53
~~SEQ ID:8~~SEQ ID NO:157	WQFSGRLEY	0	44	WQLNGRLEY	53
~~SEQ ID:9~~SEQ ID NO:158	WQFTGRLEY	0	43	WQLNGRLEY	53
~~SEQ ID:10~~SEQ ID NO:159	WQFGGRLEY	0	43	WQLNGRLEY	53
~~SEQ ID:11~~SEQ ID NO:160	WQLSGRLEY	0	48	WQLNGRLEY	53
~~SEQ ID:12~~SEQ ID NO:161	WQLTGRLEY	0	47	WQLNGRLEY	53
~~SEQ ID:13~~SEQ ID NO:162	WQLGGRLEY	0	47	WQLNGRLEY	53
~~SEQ ID:14~~SEQ ID NO:163	WQLNSQLEY	0	43	WQLNGRLEY	53

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Please replace the paragraph beginning at page 89, paragraph [0372] with the following rewritten paragraph:

--**Table 29.** Suitable less immunogenic variants of agretope 8 (residues 36-44). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 29. Suitable less immunogenic variants of agretope 8 (residues 36-44).

Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:15~~SEQ ID NO:164	QSFDIPEEI	0	39	MNFDIPEEI	48
~~SEQ ID:16~~SEQ ID NO:165	QDFDIPEEI	0	39	MNFDIPEEI	48
~~SEQ ID:17~~SEQ ID NO:166	MSFDIPEEI	0	43	MNFDIPEEI	48
~~SEQ ID:18~~SEQ ID NO:167	MTFDIPEEI	0	42	MNFDIPEEI	48
~~SEQ ID:19~~SEQ ID NO:168	MGFDIPEEI	0	42	MNFDIPEEI	48
~~SEQ ID:20~~SEQ ID NO:169	MDFDIPEEI	0	43	MNFDIPEEI	48
~~SEQ ID:21~~SEQ ID NO:170	MEFDIPEEI	0	42	MNFDIPEEI	48
~~SEQ ID:22~~SEQ ID NO:171	MNYSIPEEI	0	39	MNFDIPEEI	48
~~SEQ ID:23~~SEQ ID NO:172	MNYNIPEEI	0	40	MNFDIPEEI	48
~~SEQ ID:24~~SEQ ID NO:173	MNYEIPEEI	0	41	MNFDIPEEI	48
~~SEQ ID:25~~SEQ ID NO:174	MNYQIPEEI	0	39	MNFDIPEEI	48
~~SEQ ID:26~~SEQ ID NO:175	MNFSIPEEI	0	42	MNFDIPEEI	48
~~SEQ ID:27~~SEQ ID NO:176	MNFNIPEEI	0	43	MNFDIPEEI	48
~~SEQ ID:28~~SEQ ID NO:177	MNFEIPEEI	0	44	MNFDIPEEI	48
~~SEQ ID:29~~SEQ ID NO:178	MNFQIPEEI	0	42	MNFDIPEEI	48
~~SEQ ID:30~~SEQ ID NO:179	MNFDIPESL	0	41	MNFDIPEEI	48
~~SEQ ID:31~~SEQ ID NO:180	MNFDIPESV	0	42	MNFDIPEEI	48
~~SEQ ID:32~~SEQ ID NO:181	MNFDIPENL	0	41	MNFDIPEEI	48
~~SEQ ID:33~~SEQ ID NO:182	MNFDIPENV	0	42	MNFDIPEEI	48
~~SEQ ID:34~~SEQ ID NO:183	MNFDIPEDL	0	43	MNFDIPEEI	48
~~SEQ ID:35~~SEQ ID NO:184	MNFDIPEDV	0	44	MNFDIPEEI	48
~~SEQ ID:36~~SEQ ID NO:185	MNFDIPEQL	0	43	MNFDIPEEI	48
~~SEQ ID:37~~SEQ ID NO:186	MNFDIPEQV	0	44	MNFDIPEEI	48
~~SEQ ID:38~~SEQ ID NO:187	MNFDIPEHL	0	41	MNFDIPEEI	48
~~SEQ ID:39~~SEQ ID NO:188	MNFDIPEHV	0	42	MNFDIPEEI	48
~~SEQ ID:40~~SEQ ID NO:189	MNFDIPERL	0	41	MNFDIPEEI	48
~~SEQ ID:41~~SEQ ID NO:190	MNFDIPERV	0	42	MNFDIPEEI	48
~~SEQ ID:42~~SEQ ID NO:191	MNFDIPEKL	0	42	MNFDIPEEI	48
~~SEQ ID:43~~SEQ ID NO:192	MNFDIPEKV	0	43	MNFDIPEEI	48
~~SEQ ID:44~~SEQ ID NO:193	MNFDIPEEL	0	46	MNFDIPEEI	48

~~SEQ ID:45~~SEQ ID NO:194	MNFDIPEEV	0	47	MNFDIPEEI	48

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Please replace the paragraph beginning at page 90, paragraph [0373] with the following rewritten paragraph:

--**Table 30** Suitable less immunogenic variants of agretope 11 (residues 60-68). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 30. Suitable less immunogenic variants of agretope 11 (residues 60-68).

Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:46~~SEQ ID NO:195	HDMLQNIFA	0	38	YEMLQNIFA	46
~~SEQ ID:47~~SEQ ID NO:196	YSQLQNIFA	0	37	YEMLQNIFA	46
~~SEQ ID:48~~SEQ ID NO:197	YSLLQNIFA	0	38	YEMLQNIFA	46
~~SEQ ID:49~~SEQ ID NO:198	YSVLQNIFA	0	37	YEMLQNIFA	46
~~SEQ ID:50~~SEQ ID NO:199	YSFLQNIFA	0	37	YEMLQNIFA	46
~~SEQ ID:51~~SEQ ID NO:200	YEQLQNIFA	0	42	YEMLQNIFA	46
~~SEQ ID:52~~SEQ ID NO:201	YEMLQNIYT	0	39	YEMLQNIFA	46
~~SEQ ID:53~~SEQ ID NO:202	YEMLQNIWT	0	37	YEMLQNIFA	46
~~SEQ ID:54~~SEQ ID NO:203	YEMLQNIFT	0	42	YEMLQNIFA	46

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Please replace the paragraph beginning at page 6, paragraph [039] with the following rewritten paragraph:

--**Table 31.** Suitable less immunogenic variants of agretope 20 (residues 143-151). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 31. Suitable less immunogenic variants of agretope 20 (residues 143-151).

Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:55~~SEQ ID NO:204	WSIVRVEIL	0	42	WTIVRVEIL	46
~~SEQ ID:56~~SEQ ID NO:205	WTIVRVSIL	0	41	WTIVRVEIL	46
~~SEQ ID:57~~SEQ ID NO:206	WTIVRVEMM	0	41	WTIVRVEIL	46
~~SEQ ID:58~~SEQ ID NO:207	WTIVRVEMV	0	40	WTIVRVEIL	46
~~SEQ ID:59~~SEQ ID NO:208	WTIVRVEMF	0	39	WTIVRVEIL	46

~~SEQ ID:60~~SEQ ID NO:209	WTIVRVELF	0	40	WTIVRVEIL	46
~~SEQ ID:61~~SEQ ID NO:210	WTIVRVEVF	0	41	WTIVRVEIL	46
~~SEQ ID:62~~SEQ ID NO:211	WTIVRVEFF	0	38	WTIVRVEIL	46
~~SEQ ID:63~~SEQ ID NO:212	WTIVRVEIM	0	44	WTIVRVEIL	46
~~SEQ ID:64~~SEQ ID NO:213	WTIVRVEIV	0	43	WTIVRVEIL	46
~~SEQ ID:65~~SEQ ID NO:214	WTIVRVEIF	0	42	WTIVRVEIL	46

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Please replace the paragraph beginning at page 91, paragraph [0375] with the following rewritten paragraph:

--**Table 32.** Suitable less immunogenic variants of agretope 24 (residues 151-159). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 33. Suitable less immunogenic variants of agretope 24 (residues 151-159).

Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:66~~SEQ ID NO:215	MNNFYFINR	0	42	LRNFYFINR	49
~~SEQ ID:67~~SEQ ID NO:216	MENFYFINR	0	42	LRNFYFINR	49
~~SEQ ID:68~~SEQ ID NO:217	MQNFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:69~~SEQ ID NO:218	MHNFYFINR	0	42	LRNFYFINR	49
~~SEQ ID:70~~SEQ ID NO:219	MKNFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:71~~SEQ ID NO:220	LNNFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:72~~SEQ ID NO:221	LENFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:73~~SEQ ID NO:222	LQNFYFINR	0	45	LRNFYFINR	49
~~SEQ ID:74~~SEQ ID NO:223	LHNFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:75~~SEQ ID NO:224	LKNFYFINR	0	46	LRNFYFINR	49
~~SEQ ID:76~~SEQ ID NO:225	LRSFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:77~~SEQ ID NO:226	LRTFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:78~~SEQ ID NO:227	LRGFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:79~~SEQ ID NO:228	LRDFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:80~~SEQ ID NO:229	LREFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:81~~SEQ ID NO:230	LRQFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:82~~SEQ ID NO:231	LRHFYFINR	0	44	LRNFYFINR	49
~~SEQ ID:83~~SEQ ID NO:232	LRKFYFINR	0	43	LRNFYFINR	49
~~SEQ ID:84~~SEQ ID NO:233	LRNMYFINR	0	43	LRNFYFINR	49
~~SEQ ID:85~~SEQ ID NO:234	LRNIYFINR	0	43	LRNFYFINR	49
~~SEQ ID:86~~SEQ ID NO:235	LRNLYFINR	0	43	LRNFYFINR	49
~~SEQ ID:87~~SEQ ID NO:236	LRNFHYVNR	0	40	LRNFYFINR	49
~~SEQ ID:88~~SEQ ID NO:237	LRNFYFISQ	0	40	LRNFYFINR	49

~~SEQ ID:89~~SEQ ID NO:238	LRNFYFISK	0	41	LRNFYFINR	49
~~SEQ ID:90~~SEQ ID NO:239	LRNFYFITK	0	40	LRNFYFINR	49
~~SEQ ID:91~~SEQ ID NO:240	LRNFYFIGK	0	40	LRNFYFINR	49
~~SEQ ID:92~~SEQ ID NO:241	LRNFYFIDK	0	41	LRNFYFINR	49
~~SEQ ID:93~~SEQ ID NO:242	LRNFYFIEK	0	40	LRNFYFINR	49
~~SEQ ID:94~~SEQ ID NO:243	LRNFYFIQK	0	40	LRNFYFINR	49
~~SEQ ID:95~~SEQ ID NO:244	LRNFYFIHK	0	41	LRNFYFINR	49
~~SEQ ID:96~~SEQ ID NO:245	LRNFYFIRK	0	40	LRNFYFINR	49
~~SEQ ID:97~~SEQ ID NO:246	LRNFYFIKK	0	40	LRNFYFINR	49
~~SEQ ID:98~~SEQ ID NO:247	LRNFYFINE	0	44	LRNFYFINR	49
~~SEQ ID:99~~SEQ ID NO:248	LRNFYFINQ	0	45	LRNFYFINR	49
~~SEQ ID:100~~SEQ ID NO:249	LRNFYFINK	0	46	LRNFYFINR	49

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Please replace the paragraph beginning at page 92, paragraph [0376] with the following rewritten paragraph:

--**Table 34.** Suitable less immunogenic variants of agretope 25 (residues 154-162). B(wt) is the BLOSUM62 score of the wild type 9-mer, I(alt) is the percent of the US population containing one or more MHC alleles that are predicted to bind the alternate 9-mer at a 1% threshold, and B(alt) is the BLOSUM62 score of the alternate 9-mer.

Table 34. Suitable less immunogenic variants of agretope 25 (residues 154-162).					
Sequence ID	Variant sequence	I(alt)	B(alt)	WT sequence	B(wt)
~~SEQ ID:101~~SEQ ID NO:250	FYFISQLTG	0	40	FYFINRLTG	49

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Please replace the paragraph beginning at page 93, paragraph [0383] with the following rewritten paragraph:

--**Table 35.** Specific activity data for interferon-beta variants. The sequence for residues 5, 8, 47, 111, 116, and 120 is given for each variant, along with the total number of mutations, the EC50, and the ratio of the wild type to variant EC50. Variant IFN1_1 is the interferon beta wild type with the C17S substitution.

Table 35. Sequence and activity of interferon beta solubility variants.

SEQ ID NO	Variant	5	8	47	111	116	120	# mut	EC50 (log ng/ml)	EC50 wt / EC50 var
SEQ ID NO:15	IFN1_1	L	F	L	F	L	L	0	5.306	1.0
SEQ ID NO:49	IFB1_2	Q	F	L	F	L	L	1	0.428	12.4
SEQ ID NO:54	IFB1_7	Q	E	L	F	L	L	2	0.179	29.6
SEQ ID NO:59	IFB1_15	Q	E	L	N	L	L	3	0.319	16.6
SEQ ID NO:61	IFB1_23	Q	E	L	F	E	L	3	0.277	19.2
SEQ ID NO:71	IFB1_36	L	E	L	N	E	L	3	0.294	18.0
SEQ ID NO:73	IFB1_39	Q	E	L	N	E	L	4	0.193	27.5
SEQ ID NO:86	IFB1_64	Q	E	K	N	E	R	6	0.240	22.1

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Please replace the paragraph beginning at page 93, paragraph [0384] with the following rewritten paragraph:

-- **Table 36.** Comparison of MHC agretopes in interferon beta solubility variants. Potential agretopes that include residues that were altered in one or more of the solubility variants are shown, along with the fraction of the population for which each agretope is a hit using a 3% threshold.

Table 36. Comparison of MHC agretopes in interferon beta solubility variants

SEQ ID NO	mutations	residues	SEQ ID NO:	sequence	wt	v2	v7	v15	v23	v36	v39	v64
SEQ ID NO:251	L5Q,F8E	1 - 9	SEQ ID NO:252	MSYNLLGFL	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:253	L5Q,F8E	3 - 11	SEQ ID NO:123	YNLLGFLQR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:254	L5Q,F8E	5 - 13	SEQ ID NO:124	LLGFLQRSS	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:255	F8E	6 - 14	SEQ ID NO:256	LGFLQRSSN	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:257	F8E	8 - 16	SEQ ID NO:125	FLQRSSNFQ	0.07	0.07	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:258	L47K	40 - 48	SEQ ID NO:259	IPEEIKQLQ	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:260	L47K	44 - 52	SEQ ID NO:261	IKQLQQFQK	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:262	L47K	47 - 55	SEQ ID NO:131	LQQFQKEDA	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:263	F111N	106 - 114	SEQ ID NO:264	LEKEDFTRG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:265	F111N,L116E	111 - 119	SEQ ID NO:266	FTRGKLMSS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

SEQ ID NO:267	L116E,L120R	116 - 124	SEQ ID NO:268	LMSSLHLKR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:269	L120R	117 - 125	SEQ ID NO:270	MSSLHLKRY	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
SEQ ID NO:271	L120R	120 - 128	SEQ ID NO:272	LHLKRYYGR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

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Please insert the enclosed 145-page text entitled "SEQUENCE LISTING" immediately preceding the claims.

Amendments to the Figures:

The attached sheets of replacement formal drawings include changes to Figures 1-12. Replacement Sheet 1/13, which includes Figure 1A, replaces part of the original Figure 1 pages. Replacement Sheet 2/13, which includes Figure 1B, replaces part of the original Figure 1 pages. Replacement Sheet 3/13, which includes Figure 1C, replaces part of the original Figure 1 pages. Replacement Sheet 4/13, which includes Figure 1D, replaces part of the original Figure 1 pages. Replacement Sheet 5/13, which includes Figure 2, replaces the original Figure 2 page. Replacement Sheet 6/13, which includes Figure 3, replaces the original Figure 3 page. Replacement Sheet 7/13, which includes Figure 4, replaces the original Figure 4 page. Replacement Sheet 8/13, which includes Figures 5 and 6, replaces the original Figures 5 and 6 pages. Replacement Sheet 9/13, which includes Figures 7 and 8, replaces the original Figures 7 and 8 pages. Replacement Sheet 10/13, which includes Figures 9 and 10, replaces the original Figures 9 and 10 pages. Replacement Sheet 11/13, which includes Figures 11A and 11B, replaces part of the original Figure 11 pages. Replacement Sheet 12/13, which includes Figures 11C and 12A, replaces part of the original Figures 11 and 12 pages. Replacement Sheet 13/13, which includes Figures 12B and 12C, replaces part of the original Figure 12 pages.